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Standardised Frailty Indicator as Predictor for Postoperative Delirium after Vascular Surgery: A Prospective Cohort Study

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Abstract *Objectives:* To determine whether the Groningen Frailty Indicator (GFI) has a positive predictive value for postoperative delirium (POD) after vascular surgery.
Methods: Between March and August 2010, 142 consecutive vascular surgery patients were prospectively evaluated. Preoperatively, the GFI was obtained and postoperatively patients were screened with the Delirium Observation Scale (DOS). Patients with a DOS-score $\geq$3 points were assessed by a geriatrician. Delirium was defined by the DSM-IV-TR criteria. Primary outcome variable was the incidence of POD. Secondary outcome variables were any surgical complication and hospital length of stay (HLOS) (>7 days).
Results: Ten patients (7%) developed POD. The highest incidence of POD was found after aortic surgery (17%) and amputation procedures (40%). Increased comorbidities ($p = 0.006$), GFI score ($p = 0.03$), renal insufficiency ($p = 0.04$), elevated C-reactive protein ($p = 0.008$), high American Society of Anaesthesiologists score ($p = 0.05$), a DOS-score of $\geq$3 points ($p = 0.001$), post-operative intensive care unit admittance ($p = 0.01$) and HLOS $\geq$7 days ($p = 0.005$) were risk factors for POD. The GFI score was not associated with a prolonged HLOS. A mean number of 2 ± 1 (range 0—5) complications were registered. The receiver operator characteristics (ROC) area under the curve for the GFI was 0.70.
Conclusions: The GFI can be helpful in the early identification of POD after vascular surgery in a select group of high-risk patients.

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Postoperative delirium (POD) is a common and serious complication after surgery. It is defined as an acute disorder of attention and cognition and is characterised by fluctuating symptoms of inattention, disturbance of consciousness and disorganised thinking.[1] Not only does it affect approximately 11–24% of elderly patients on hospital admission, it is also associated with longer hospitalisation and institutionalisation, higher medical costs, persistent functional decline and even death.[1–7] With the elderly population increasing at an unprecedented rate, the number of surgical procedures in the elderly will increase in the future. Therefore, the incidence of POD is also likely to increase, unless preventive strategies are developed. The first crucial step in delirium prevention is the identification of those patients most at risk for POD. From various studies focussing on POD among surgical patients, it is known that vascular surgery patients, especially after aortic surgery, are at highest risk for developing POD.[1] This seems primarily determined by both advanced age and the tendency to have multiple comorbidities, including cerebrovascular disease. Notwithstanding this increased incidence, very few studies focus on risk factors and delirium prevention among vascular surgery patients and an accurate pre-screening tool is currently lacking.[8–12] At the University Medical Center Groningen, the Groningen Frailty Indicator (GFI) had been developed to identify patients at risk for POD and other adverse outcomes.[13] The GFI is a simple questionnaire consisting of 15 items which are classified into eight separate groups, consistent with the domains of functioning (Table 1). A score of four or more indicates a higher risk for frailty and possible delirium. Although the GFI has been primarily designed for onco-geriatric surgical patients and has already been validated in various publications and among different patient groups, including traumatology, pulmonology, oncology and internal medicine patients, to date the GFI has not been tested among vascular surgery patients.[14–19] The purpose of this prospective cohort study was to determine whether the GFI has a positive predictive value for POD and other surgical complications in vascular surgery patients and could potentially be used as a screening tool to identify patients at high risk for POD.

Materials and Methods

Between March and August 2010, a total of 142 consecutive vascular surgery patients were prospectively evaluated. All vascular surgery patients admitted and/or operated in an elective setting, regardless of age or co-morbidity, were included. All patients were examined both pre- and post-operatively. Preoperatively, the GFI was obtained at the surgical outpatient clinic by specially trained nurses. During admission, all patients were observed by nurses trained for this study during three shifts. When POD was highly suspected, the ward doctor was informed and further assessment was done by using the delirium observation screening scale (DOS). The DOS consists of 13 items that can be rated as absent or present and describes typical behavioural patterns related to delirium.[20,21] Three or more points were considered indicative of delirium. When delirium was present or suspected, a geriatrician was consulted and the diagnosis was confirmed based on the DSM-IV-TR criteria.[22] Medical co-morbidity was quantified using the Charlson comorbidity index (CCI).[23] As such, each medical condition was assigned a weighted score, range 0–19. Based on these comorbidities, the CCI predicts the 1-year mortality. Apart from the GFI and DOS, routine clinical data were recorded pre-, intra- and postoperatively. The following predictors were investigated: preoperative predictors such as age and sex, American Society of Anaesthesiologists score (ASA), haemoglobin level, impaired renal function (glomerular filtration rate (GFR) <60 ml min^{-1} $\times$ 1.73 m^2), C-reactive protein (CRP), and leucocyte count; intra-operative predictors such as estimated blood loss, type of surgical procedure and type of anaesthesia; and post-operative predictors and outcomes such as intensive care unit (ICU) admittance, hospital length of stay (HLOS), psychoactive drug administration (in case of POD) and all medical complications that occurred during hospitalisation. Surgical complications and deaths were identified and classified according to a system proposed by Clavien and associates.[24,25] The Clavien–Dindo classification of surgical complications is a validated system that correlates with both the complexity of the procedure as well as HLOS. Complications are graded from 1 to 6 and range from minor complications without the need for intervention (1) to the death of a patient (6). The primary outcome variable was the incidence of POD. Secondary outcome variables were any (post-operative) surgical complication and HLOS ($>$7 days). This study was approved by the Institutional Review Board. All patients gave informed consent.

Statistical Analyses

Differences between categorical variables that were possibly related to the development of POD were tested with Pearson's χ^2 test (two variables). Differences between numerical variables were tested with Student's two-tailed test (normally distributed continuous variables) or, if appropriate, Mann–Whitney *U* test (skewed continuous variables). Skewed continuous variables are shown as median (interquartile range). Variables associated with outcome POD and statistically significant with univariate analysis were entered into multivariate logistic regression analysis using a simultaneous forced entry model (Enter method). We used a probability for stepwise entry of $p < 0.05$ and a probability of removal of $p < 0.10$. The GFI was plotted in a receiver operator characteristics (ROC) curve. Two-tail *P*-values were used throughout and significance was set at $p < 0.05$. Data are presented as means $\pm$ standard deviation, unless stated otherwise. All statistical analyses were done with the Statistical Package for the Social Sciences (SPSS 16.0.1, SPSS, Chicago, IL, USA, 2007).

Results

A total of 142 patients were included in the study and further analyzed. The mean age of the total cohort was 68 $\pm$ 11 years (21–87). There was an unequal distribution in sex with 100 men (70%) and 42 women (30%). Patient characteristics and demographic data are shown in Table 2.

Table 1 The Groningen Frailty Indicator (GFI).

	Yes	No	Sometimes
	YES		NO
Mobility			
Can the patient perform this task without any help? (using tools like walking sticks, wheelchairs or walker is regarded as independent)			
1. Go shopping		0	1
2. Walk around outside (around the house or to neighbours)		0	1
3. Dressing and undressing		0	1
4. Toilet visit		0	1
Vision			
5. Does the patient experience problems in daily life by poor vision?		1	0
Hearing			
6. Does the patient experience problems in daily life by poor hearing?		1	0
Nutrition			
7. Has the patient involuntarily lost weight ($\geq$6 kg) in the past 6 months (or $\geq$3 kg in one month)		1	0
Co-morbidity			
8. Does the patient currently use four or more different types of medication?		1	0
	Yes	No	Sometimes
Cognition			
9. Does the patient currently has complaints about his memory (or has a history of dementia)	1	0	0
Psychosocial			
10. Does the patient sometimes experience emptiness around him?	1	0	1
11. Does the patient sometimes miss people around him?	1	0	1
12. Does the patient sometimes feel abandoned?	1	0	1
13. Has the patient recently felt sad or depressed?	1	0	1
14. Has the patient recently felt nervous or anxious?	1	0	1
Physical fitness			
15. Which grade would the patient give its physical fitness (0–10, ranging from very bad to good) 0–6 = 1 7–10 = 0	1	0	
Total score GFI			

A score of four or more indicates a higher risk for frailty and possibly delirium.

Ten patients (7%) developed POD. The highest incidences were found after open aortic surgery (30%) and amputation procedures (40%). Types of surgery with concomitant POD incidences are shown in Table 3.

Groningen Frailty Indicator as predictor for POD

A total of 50 patients (35%) scored a GFI of $\geq$4 points. The predictive value of the GFI was assessed with univariate analyses. A GFI score $\geq$4 points was significantly related with the development of POD ($p = 0.03$). The ROC curve for GFI as predictor for delirium is shown in Fig. 1. The area under the curve was 0.70 with the GFI set at $\geq$4 as indicative of an increased risk for POD (sensitivity 50%, specificity 78%). With the GFI cut-off point adjusted to $\geq$6 points, the area under the curve increased to 0.89 (sensitivity 50%, specificity 86%).

GFI as predictor for post-operative complications and HLOS

Complications were recorded using the Clavien–Dindo classification. A total of 33 complications were registered (range 0–5). Grades 1 and 2 were most frequently recorded (Table 1). The GFI score was not a predictive factor for the development of complications ($p = 0.83$). Also, the number of complications were not significantly related to the development of POD ($p = 0.37$). The GFI score was not associated with a prolonged HLOS with a mean HLOS for GFI <4 of 5.4 $\pm$ 3.9 days vs. 5.9 $\pm$ 4.2 days for a GFI $\geq$4 ($p = 0.71$).

Additional predictive factors for POD

Univariate analysis yielded various factors that were associated with the development of POD. These factors included the number of comorbidities ($p = 0.006$), impaired renal function (glomerular filtration rate (GFR) <60 ml min^{-1} $\times$ 1.73 m^2) ($p = 0.04$), elevated C-reactive protein (CRP) ($p = 0.008$), high American Society of Anesthesiologists (ASA) score ($p = 0.05$) and a DOS-score of $\geq$3 points ($p = <0.005$). In terms of outcome parameters, both post-operative ICU admittance ($p = 0.01$) and HLOS $\geq$7 days ($p = 0.005$) were associated with the development of POD (Table 4). Although age alone appeared to have no significant relation to POD, high age (>65 years) did account for >75% of all complications. Multivariate logistic regression analyses on the factors significantly associated

Table 2 Patient characteristics and demographic data.

Parameter	Number or mean ± SD[a] (Percentage or range)
Number (%)	142 (100)
Age (years)	68 ± 11 (21–87)
Gender	
Men	100 (70)
Women	42 (30)
Delirium	10 (7.0)
GFI ≥4[b]	50 (35.2)
Comorbidities (CCI)[c]	5 ± 2 (1–14)
Blood loss (ml)	386 ± 802 (0–3500)
Impaired renal function[d]	16 (11)
Pre-operative haemoglobin (mmol/l)	8.4 ± 1.2 (4.7–11.1)
C-reactive protein (mg/dl) (median, IQR)[e]	5 (5–13)
ASA[f]	2.6 ± 0.6 (1–4)
ICU admittance (no of patients)	23 (16)
Hospital length of stay (days)	5.6 ± 4 (1–30)
Complications[g]	1.8 ± 1.3 (range 0–5)

[a] Standard deviation.
[b] Groningen Frailty Indicator, a score of four or more indicates a higher risk for frailty and possibly delirium.
[c] Charlson comorbidity index, a weighed index which measures the burden of comorbidities and predicts 1-year mortality (range 0–19 indicating respectively no comorbidities to considerable comorbidities).
[d] Defined as glomerular filtration rate (GFR) <60 ml/min × 1.73 m^2.
[e] CRP level >5 mg/dl as measured preoperatively.
[f] American Society of Anaesthesiologists score (assesses the fitness of patients prior to surgery, 1 = a normal healthy patient and 5 = a moribund patient who is not expected to survive without the operation).
[g] According to the Clavien–Dindo classification of surgical complications Complications are graded from 1 to 6 and range from minor complications without the need for intervention (1) to the death of a patient (6).

with POD in univariate analyses identified no independent risk factors for POD. However, there was a trend towards statistical significance for the GFI (OR 1.9, 95% CI 0.98–3.77) (Table 5).

Table 3 Types of surgical procedures with concomitant postoperative delirium incidences.

Type of procedure	Number of patients (%)	Delirium present (%)
Open aortic surgery	18 (12.7)	3 (30)
Endovascular procedures	30 (21.1)	2 (20)
Peripheral bypass surgery	39 (27.5)	0
Arteriovenous shunt surgery	2 (1.4)	0
Percutaneous interventions	27 (19.0)	0
Amputation surgery	10 (7.0)	4 (40.0)
Miscellaneous	16 (11.3)	1 (10)
Total	142 (100)	10 (100)

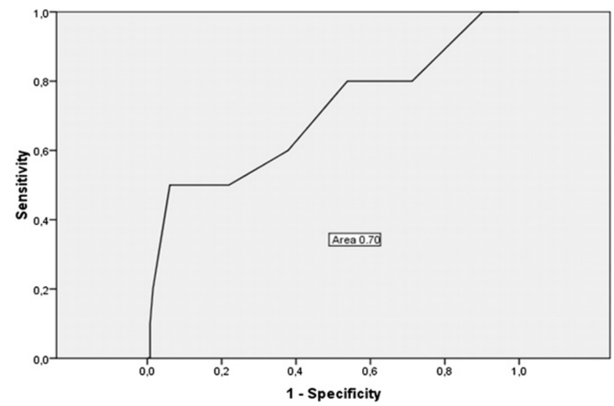

Figure 1 Receiver operator characteristics (ROC) curve for the GFI as predictor for delirium in 142 patients undergoing elective vascular procedures. The area under the curve is 0.70 with the GFI set at ≥4 as indicative of an increased risk for POD (sensitivity 50%, specificity 78%). With a GFI cut-off point of ≥6 points, the area under the curve increased to 0.89 (sensitivity 50%, specificity 86%).

Factors and outcome parameters significantly associated with a DOS-score of ≥3 points were the number of comorbidities ($p = 0.04$) and increased CRP levels ($p = 0.01$) and an extended HLOS ≥7 days ($p = 0.02$) (Table 6).

Discussion

This study shows the predictive value of the GFI in the development of POD after elective vascular surgery in a heterogeneous patient population. Although many studies have identified risk factors for delirium, this study provides the physician with the ability to be informed about the risk very early in the treatment process. By starting preventive treatments or aggressive assessment during hospitalisation in patients with a GFI ≥4 points, we believe that this could reduce the incidence of POD and perhaps, ultimately, HLOS. In this context, both the British Geriatric Society and Dutch Professional Guideline have set up useful clinical guidelines to prevent and treat delirium which could be converted to a clinical roadmap and added to the clinical chart of these high-risk patients.[26,27] A Cochrane database systematic review on delirium prevention has already proven that both active geriatric consultation and low dose haloperidol medication in high-risk post-operative patients may reduce the degree and duration of POD.[28]

In addition to the GFI score, pre-existing comorbidities, an elevated CRP and ICU admittance were associated with an increased risk for POD in univariate analysis. These factors have been reported previously as risk factors for POD and confirm that our studied cohort corresponds with similar studies on POD.[2,7,11,29,30] Contrary to the literature, age was not a predictor for POD in the current study but this may be the result of the limited number of patients in the studied cohort.

There are several drawbacks in this study that need to be addressed. We found an unexpected and relatively low delirium incidence despite increased awareness and DOS assessment. In the current literature, POD incidences after elective vascular surgery vary from 23% to 39%.[8–12] The

Table 4 Univariate analysis with prevalence and median values of risk factors for the development of postoperative delirium.

Variable	Predictor available (100%)	Delirium present	Delirium absent	P^a
Age (mean ± SD)	142	73 ± 10	68 ± 11	0.200
Female gender	142	1 (10.0%)	41 (31.1%)	0.281
Comorbidities (CCI)[b]	142	7.0 ± 2.2	5.0 ± 2.2	0.006
Hemoglobine (mg/ml)	107	7.4 ± 1.8	8.5 ± 1.1	0.156
Impaired renal function[c]	135	3 (33.3%)	13 (10.3%)	0.04
C-reactive protein, median (IQR)	65	5 (5–9)	149 (52–219)	0.008
Leukocyte count	67	11.8 ± 6.1	8.2 ± 2.3	0.207
ASA-score >2[d]	142	9 (90%)	79 (59%)	0.05
Blood loss (ml), median (IQR)	65	350 (13–3250)	63 (0–188)	0.15
Hospital length of stay, median (IQR)	142	10 (6–15)	4 (3–7)	0.005
ICU-admittance	142	4 (44%)	19 (14.1%)	0.02
DOS-score >3[e]	46	4 (100%)	1 (2.4%)	<0.005
GFI score, median (IQR)[f]	142	5.5 (2.5–7.5)	3 (1–4)	0.03

Results reported as number.
IQR = interquartile range.
[a] *p*-values ≤0.05 were considered statistically significant.
[b] Charlson comorbidity index, a weighed index which measures the burden of comorbidities and predicts 1-year mortality (range 0–19 indicating respectively no comorbidities to considerable comorbidities).
[c] Defined as glomerular filtration rate (GFR) <60 ml/min × 1.73 m^2.
[d] American Society of Anesthesiologists (assesses the fitness of patients prior to surgery, 1 = a normal healthy patient and 5 = a moribund patient who is not expected to survive without the operation).
[e] Delirium Observation Screening scale. Consists of 13 items, ≥3 points were considered indicative for delirium.
[f] Groningen Frailty Indicator, a score of ≥4 indicates higher risk for frailty and possibly delirium.

reported rate in our study may be low as a result of the increased awareness of signs of POD amongst the nursing staff in the participating wards. It is a known effect that increasing awareness of signs of delirium decreases the incidence of full-blown POD. It is, however, not an uncommon finding that delirium incidence is low in specific prevalence studies. In a large prospective cohort study by Marcantonio et al., postoperative delirium occurred in only 117/1341 (9%) patients older than 50 years, which confirms that the incidence does not entirely depend on group size.[31] Although we know from several studies focussing on delirium prevention that high age is a risk factor for POD, we included all age groups who underwent elective vascular surgery to reliably estimate the value of the GFI in this cohort of patients. We feel this was a justified choice as the vascular patient in itself is frailer than general surgical patients and thus possibly more prone to develop POD. This has led to a diverse patient population with a mean age of 68 ± 11 (range 21–87). Even though the GFI score was not a predictor for post-operative complications, high age (>65 years) did account for >75% of all complications. Furthermore, although the GFI seems to provide a good estimate of the risk for POD, it is probably not reliable in a younger (<65 years) patient group.

Table 5 Multivariate analysis of risk factors for the development of postoperative delirium.

Variable	Odds ratio	95% Confidence interval	*P*
GFI-score	1.9	0.9–3.7	0.05
Comorbidities (CCI)[a]	0.9	0.5–1.7	0.84
C-reactive protein	1.0	0.9–1.0	0.19

[a] Charlson comorbidity index, a weighed index which measures the burden of comorbidities and predicts 1-year mortality (range 0–19 indicating respectively no comorbidities to considerable comorbidities).

In multivariate analyses the problem of underfitting occurred in our model. For a credible risk estimate, a ratio of 10 events per independent variable is suggested. Because of the unexpected low POD incidence in our study, this ratio could unfortunately not be met in the current model. This means that the outcome for individual variables may not be trustworthy.[32] Consequently, although a trend towards statistical significance was suggested, neither the GFI nor the other independent risk factors reached a significant outcome in the multivariate model.

We would have strongly preferred that all patients had undergone a proper DOS assessment. Unfortunately, because of logistical problems, we had to choose the current alternative with DOS assessment only in cases when suspicion for POD was high. This may have led to an underestimation of delirium incidence by missing clinical subtypes such as hypoactive delirium or the unclassified type which account for respectively 29% and 7% of delirium subtypes.[3] Despite the predictive value of the GFI score, the area under the curve was only 0.70 with the GFI score set at ≥4 but increased to 0.89 after adjusting the GFI cut-off point to 6 points. Whereas a score of ≥4 was chosen for frail patients in general, this cut-off score was determined by previous publications.[14–19] This is the first study in which

Table 6 Univariate analysis with prevalence and median values of risk factors for an increased DOS-score.[a]

Variable	Predictor available (100%)	DOS-score <3	DOS-score ≥3	P^b
Age	142	69 ± 8.7	74 ± 7.1	0.269
Female gender	142	10 (100%)	0 (0%)	0.570
Comorbidities (CCI)[c]	142	5.1 ± 1.9	7.1 ± 1.6	0.04
Hemoglobine (mg/ml)	107	8.2 ± 1.0	6.7 ± 1.5	0.09
Impaired renal function[d]	135	5 (71.4%)	2 (28.6%)	0.173
C-reactive protein, median (IQR)	65	5 (5–11.75)	98 (44–182)	0.01
Leukocyte count	67	8.1 ± 2.8	12.9 ± 8.2	0.419
ASA-score >2[e]	142	27 (78.1%)	4 (12.9%)	0.524
Blood loss (ml), median (IQR)	65	87.5 (0–500)	300 (162–1900)	0.406
Hospital length of stay, median (IQR)	142	5 (4–7)	8 (7–22)	0.017
ICU-admittance	142	6 (75%)	2 (25%)	0.158
GFI score, median (IQR)[f]	142	3 (2–4.5)	3 (1–8.5)	0.803

Results reported as number.
IQR = interquartile range.
a Delirium Observation Screening scale. Consists of 13 items, ≥3 points were considered indicative for delirium.
b *p*-values ≤0.05 were considered statistically significant.
c Charlson comorbidity index, a weighed index which measures the burden of comorbidities and predicts 1-year mortality (range 0–19 indicating respectively no comorbidities to considerable comorbidities).
d Defined as glomerular filtration rate (GFR) <60 ml/min × 1.73 m^2.
e American Society of Anesthesiologists (assesses the fitness of patients prior to surgery, 1 = a normal healthy patient and 5 = a moribund patient who is not expected to survive without the operation.).
f Groningen Frailty Indicator, a score of ≥4 indicates higher risk for frailty and possibly delirium.

the GFI score was tested in vascular surgery patients. Within the GFI questionnaire, points are given which are consistent with the domains of functioning. Vascular surgery patients are generally considered a group with limited mobility and therefore get points awarded which are not directly related to frailty. It, therefore, may very well be possible that the cut-off score should be adjusted in this patient group. But more likely is that the GFI in its current form may not apply to the entire cohort of patients undergoing vascular surgery. In order to determine its true value in POD risk assessment after vascular surgery, an adjusted score must be used in this specific cohort. In a subsequent study, a modified score shall be used which will be applied to the group at highest risk for POD (age ≥65 years, aortic surgery and amputation procedures).

In conclusion, this prospective study shows that the GFI, with its limitations, can be helpful in the early identification of a select group of high-risk patients with respect to the development of delirium after vascular surgery. Despite a range of publications on pre- and post-operative risk factors for POD, a preoperative tool for risk assessment is not yet at hand. By using the GFI to identify these patients during the preoperative outpatient evaluation, appropriate preventive arrangements, such as preoperative geriatric consultation, can be implemented. In this way HLOS, medical costs and further institutionalisation (due to functional loss, loss of independence and the inability to return to their homes) can potentially be reduced. However, the applicability within the entire cohort of vascular surgery patients can be further improved based on this implementation study.

Conflict of Interest/Funding

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